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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/339,103 06/24/99 KILGER

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ARENT FOX KINTNER PLOTKIN & KAHN
1050 CONNECTICUT AVENUE, N.W.
SUITE 600
WASHINGTON DC 20036

EXAMINER

HORLICK, K

ART UNIT

PAPER NUMBER

1656

15

DATE MAILED:

10/02/01

~~Please find below and/or attached an Office communication concerning this application or proceeding.~~

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/339,103

Applicant(s)

KILGER ET AL.

Examiner

Kenneth R Horlick

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 September 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-126 and 132-145 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-126 and 132-145 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 08/991,184.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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1. The request filed on 09/10/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/339,103 is acceptable and a CPA has been established. An action on the CPA follows.

2. Claims 133 and 142 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are confusing because of improper Markush language ("or" rather than "and").

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-126, 134-137, and 143-145 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34-58 of copending Application No. 09/357,166 in view of Gelfand et al. (US 5,310,652) and Birch et al. (5,677,152). This is a provisional obviousness-type double

patenting rejection.

The copending claims are drawn to methods and kits for simultaneously amplifying and sequencing nucleic acids, requiring two different polymerases, wherein one has a higher affinity towards a chain-terminating nucleotide relative to the other.

The copending claims do not encompass direct application of the methods/kits to RNA wherein at least one of the polymerases has reverse transcriptase activity, nor modification of said methods/kits to include a polymerase-inhibiting agent.

Gelfand et al. disclose a one-tube, one-polymerase amplification of target RNA sequences using a polymerase with reverse transcriptase activity (see, for example, the abstract).

Birch et al. disclose the advantageous use of a polymerase-inhibiting agent, including antibodies and various anhydrides, in nucleic acid amplifications (see, for example, the abstract and Fig. 1).

One of ordinary skill in the art would have been motivated to modify the methods of the copending claims by application towards RNA using a polymerase with reverse transcriptase activity, and/or application of a polymerase-inhibiting agent, because Gelfand et al. disclosed the advantages of combined reverse-transcription and

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amplification, and Birch et al. disclosed the benefits of using such an agent in amplification reactions. In other words, these would have been logical, straightforward applications to achieve expected improvements. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed kits and carry out the claimed methods.

4. Claims 138-140 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34, 37, and 38 of copending Application No. 09/577,047. This is a provisional obviousness-type double patenting rejection. Both sets of kit claims overlap in subject matter, particularly with respect to inhibiting reagents for two different polymerases.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.

Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

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not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-126, 134-137, and 143-145 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koster et al. (US 5,928,906) in view of Gelfand et al. (US 5,310,652) and Birch et al. (5,677,152).

These claims are drawn to methods and kits for simultaneously amplifying and sequencing nucleic acids, requiring two different polymerases, wherein one has a higher affinity towards a chain-terminating nucleotide relative to the other, further comprising: direct application to RNA wherein at least one of the polymerases has reverse transcriptase activity; and/or use of a polymerase-inhibiting agent.

Koster et al. disclose methods and kits for simultaneously amplifying and sequencing nucleic acids, requiring two different polymerases, wherein one has a higher affinity towards a chain-terminating nucleotide relative to the other (see especially column 3, lines 25-57, column 7, lines 43-67 and column 8, lines 1-6, and Example 1 in columns 11-12).

This patent does not disclose DNA polymerase-mediated reverse transcription coupled to PCR amplification, nor the use of polymerase-inhibiting agents.

Gelfand et al. disclose a one-tube, one-polymerase amplification of target RNA

sequences using a DNA polymerase with reverse transcriptase activity (see, for example, the abstract).

Birch et al. disclose the advantageous use of a polymerase-inhibiting agent, including antibodies and various anhydrides, in nucleic acid amplifications (see, for example, the abstract and Fig. 1).

One of ordinary skill in the art would have been motivated to modify the method of Koster et al. by application towards RNA using a polymerase with reverse transcriptase activity, and/or application of a polymerase-inhibiting agent, because Gelfand et al. disclosed the advantages of combined reverse-transcription and amplification, and Birch et al. disclosed the benefits of using such an agent in amplification reactions. In other words, these would have been logical, straightforward applications to achieve expected improvements. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed kits and carry out the claimed methods.

6. Claims 132, 133, 141, and 142 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koster et al. (US 5,928,906) in view of Gelfand et al. (US 5,310,652) and Birch et al. (5,677,152), and further in view of Hill (US 5,525,492).

The further limitations of these claims involve agents that lower the melting point of DNA, which is not taught in the previously-discussed references.

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Hill discloses the use of a polar aprotic solvent such as DMSO in nucleic acid amplification reactions to facilitate amplification of G-C rich sequences (see column 2, lines 5-40).

One of ordinary skill in the art would have been motivated to use a melting point-lowering agent such as DMSO in the methods and kits as rejected previously because Hill taught that this advantageously provided for amplification of sequences of high G-C content. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed kits and carry out the claimed methods.

7. Claims 138-140 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koster et al. (US 5,928,906), further in view of Birch et al. (US 5,677,152) and Scalice et al. (US 5,338,671).

These claims are drawn to kits as described above, further comprising a polymerase-inhibiting agent X, such that said agent X and another polymerase-inhibiting agent can inhibit different polymerases.

The primary reference is discussed above.

This reference does not teach polymerase inhibition.

Birch et al. disclose the advantages of initial inhibition of polymerase by chemical modification.

Scalice et al. disclose the advantages of initial inhibition of polymerase by antibodies.

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One of ordinary skill in the art would have been motivated to combine the reagents used in the method of Koster et al., including primers and the two different thermostable polymerases, into a kit, because such kits were well known and common knowledge in the art for facilitating the practice of methods requiring a given set of reagents. The skilled artisan would have been further motivated to add one or two polymerase-inhibiting reagents to such a kit because the advantage of initially inhibiting polymerases in amplification reactions was disclosed by Birch et al. and Scalice et al., which taught the use of two different types of inhibiting agents (chemical and antibody, respectively). It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make the claimed kits.

8. No claims are free of the prior art.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kenneth R Horlick whose telephone number is 703-308-3905. The examiner can normally be reached on Monday-Thursday 6:30AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on 703-308-. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-0294 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Kenneth R. Horlick, M.D.

Kenneth R Horlick
Art Unit 1656

September 19, 2001

**KENNETH R. HORLICK
PRIMARY EXAMINER
GROUP 1600**